REMARKS

Claims 1-13 are pending in the application. Claims 1, 5 and 9 are amended. Support for the amendments can be found in paragraph [0005], [0019] and [0021] of the U.S. published application no. 2007/0065493 A1, which is the publication of the present application. New claim 13 is added. Support for the relative amounts of polyvinylpyrrolidone and estrogen can be found in paragraph [0021].

Claim Objections

As stated by the Examiner, claim 5 was incorrectly identified as "currently amended" in the last response. It was a typographical error.

The Examiner also suggested: "[t]he components are also all identified as a. It is suggested Applicant amend the claim to recite components a-d." The "a" was actually being used simple as the article "a" in claim 5. Since apparently it looked like the "a" was being used to list the components, claim 5 and similar claim 9 have been amended to recite the components as a-e. This amendment is being made just for stylistic and reading ease and does not change the scope of the claims in any way.

Claim Rejections – 35 USC § 103

Features of the present invention

The present invention relates to an external patch comprising a backing and an adhesive layer laminated onto the backing, the adhesive layer containing as essential components a 5 to 50 wt% styrene-isoprene-styrene block copolymer (SIS), a 20 to 70 wt% rosin-based resin, a 10 to 60 wt% softener, especially polybutene or liquid paraffins, and a 1 to 20 wt% polyvinylpyrrolidone, along with estrogen and/or progestogen as active ingredients.

The adhesive base material of the external patch contains the rosin-based resin as the adhesive resin and thereby the crystallization of progestogen in the base patch material is reduced. Specifically, the rosin-based resin is used for dissolving progestogen

and for preventing the crystallization of progestogen in the adhesive base material. See paragraph [0019] of the U.S. published application no. 2007/0065493 A1, which is the publication of the present application.

In addition, polyvinylpyrrolidone is used for dissolving estrogen and is used for preventing the crystallization of estrogen in the adhesive base material. See paragraph [0021]. The use of polyvinylpyrrolidone as a dissolving component in the present application is contrary to the common use of polyvinylprrolidone in the pharmaceutical field as a binding or suspending agent. The claims have been amended so all of the independent claims recite both rosin-based resin and polyvinylpyrrolidone, as a dissolving agent.

Furthermore, the softener, along with the SIS, rosin-based resin and polyvinylpryrolidone, also aid in dissolving the estrogen/progesterone active ingredient and helps improve the ability of the patch to follow the irregularities of the skin surface. See paragraph [0020]. All together, in applicants' external patch, the crystallization of the drug in the base material is reduced, stable drug release is ensured, and there is little irritation to the skin. All of these improvements using the components taught by the applicants are not shown in the prior art as will be discussed below.

1. Claims 1-3, 5-7, and 9-11 were rejected as being unpatentable over Hirano et al. (JP 11-001441) of record, in view of Grawe (US Patent 6,902,741).

The Examiner maintains that it is obvious for one of ordinary skill in the art at the time the invention was made to use the 17-beta-estradiol taught by Grawe et al. in the formulation of Hirano et al. since they are disclosed to be functional equivalents. Grawe et al. additionally discloses the use of the hydrophilic non-cross linked polymer, which allows for high, active substance loading and good storage stability.

The invention of Hirano relates to a percutaneously absorbable preparation characterized in that the preparation uses styrene-isoprene-styrene block copolymer

(SIS), a softener, a tackifying resin and hexylene glycol as the ingredients for the substrate composition for the active ingredient to be percutaneously absorbed. Estrogen is suggested as an active ingredient.

The specific feature of the invention of Hirano is using hexylene glycol as an absorption accelerating agent and/or solubilizer for a pharmaceutical ingredient. Hexylene glycol has known uses as a moisturizer and an antibacterial agent in cosmetic material. See paragraph [0004] of Hirano et al. In Hirano et al., the hexylene glycol is used as an absorption accelerating agent and/or a solubilizer for pharmaceutical ingredients and is therefore an essential component of Hirano. There is nothing in Hirano et al. or the newly cited reference, Grawe et al., which would suggest the elimination of hexylene glycol. Hexylene glycol is a key element of the Hirano reference. See paragraphs [0013] and [0014] of Hirano. The preparation disclosed in the Hirano reference would not even be an attractive starting material for experimentation, since hexylene glycol is a diol and like another alcohol, ethanol, is an irritant. See paragraph [0005] of the published application. One of the advantages of the preparation of the present application is reduced skin irritation as shown in Table 4. See paragraphs [0044] and [0045] of published application.

The invention of Grawe et al. relates to a transdermal system, which includes a sex hormone-containing adhesive matrix, which contains inclusions of a sex hormone in a hydrophilic non-crosslinked polymer. The purpose of the invention of Grawe et al. is to provide active substance-containing laminates for transdermal systems that are capable of exhibiting high active substance loading and good storage stability. "This objective is reached by use of an active substance inclusion consisting of a hydrophilic non-crosslinked polymer and an active substance included in said polymer, and a polymeric adhesive matrix into which said included active substance is incorporated." See col. 3, lines 36-46 of the Grawe et al. patent. One choice for the hydrophilic, non-crosslinked polymer is polyvinylpyrrolidone. Therefore, the interaction between the active ingredient and polyvinylpyrrolidone is quite different in the Grawe et al. patent as compared to the

adhesive layer of the present application. In the present application, the polyvinylpyrrolidone is used to dissolve the hormone, not as a "polymer for inclusion." "Polyvinylpyrrolidone, as a dissolving component" is clearly stated in the claims as amended.

Moreover, according to the invention of Grawe et al., the form of the active substance is preferably amorphous to an extent of more than 50 wt.% and it is particularly preferred if the form of the active substance contained in the inclusion is amorphous to an extent of more than 95 wt.%. See col. 3, lines 59-63 of Grawe et al. On the contrary, in the present application, the polyvinylpyrrolidone in the adhesive layer of the present invention serves as a component in which to dissolve estrogen. In applicants' disclosure, the amount of polyvinylpyrrolidone is preferably two times or more, and more preferably five times the amount of estrogen. New claim 13 specifically claims this higher amount.

2. *Claims 4, 8 and 12 were also rejected as being unpatentable over Hirano et al. (JP 11-001441) of record, in view of Grawe et al. (US Patent 6,902,741) and further in view of Azuma et al. (US Patent 5,200,190).*

The same arguments apply to this rejection as discussed above. Since the adhesive layer of the present application is unobvious over the teaching Hirano in view of Blank, applicants respectively submit that the additional element of the backing is not relevant.

Nonetheless, the Examiner further maintained that even though the thickness of the layers were not disclosed, it would have been obvious to prepare a film in varying thickness based on the needs of the patch. However, applicants respectfully submit that the concrete example of the Azuma et al. patch discloses only a single layer of polyethylene terephthalate having a thickness of 38 μm, and there is no description or suggestion of a laminated backing which comprises both a 0.1 to 20 μm thick

polyethylene terephthalate film and 1 to 200 μm thick flexible polymer film, nonwoven fabric or woven fabric of the present invention.

Moreover, in applicants' disclosure, the polyethylene terephthalate film layer acts as the drug non-absorptive layer, and this drug non-absorptive layer is laminated with flexible film that can closely follow the irregularities of the skin surface as well as the movement of the skin. As taught by applicants, these flexible films may be polymer films, nonwoven fabrics or woven fabrics having a thickness of 1 to 200μm to comprise the backing of the external patch of the present invention.

Applicants respectfully submit that there is no suggestion of all the elements in the claims of the present invention, as amended and currently pending, in the prior art references and no reason why a person of ordinary skill would combine these elements in the advantageous manner taught only by applicants. Both references teach estrogen delivery systems. There is no reason to rearrange and combine elements to achieve the prevent invention. Applicants respectfully maintain that the claims as filed and amended are in condition for allowance.

CONCLUSION

If the Examiner has any questions or suggested Examiner's amendments, the Examiner is respectfully requested to call the undersigned.

The Commissioner is hereby authorized to charge any additional fees, or to credit any overpayment, to Deposit Account No. 50-3195.

Respectfully submitted,

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